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(54) Title: CONTACT LENS CLEANING SOLUTION BASED ON QUATERNARY AMMONIUM PHOSPHATE ESTERS			
(57) Abstract			
<p>Method of using and composition for a contact lens cleaning, disinfecting, and rinsing solution containing a non-ionic surfactant, a triquaternary phosphate ester, disodium edentate and other additives. The non-ionic surfactant is a block copolymer of polyoxypropylene and polyoxethylene when blended with the triquaternary phosphate ester produces a potentiated effect in its anti-microbial activities in the treatment of <i>S. marcescens</i>. The resulting solution has superior cleaning, greatly improved anti-microbial and low cytotoxicity properties.</p>			

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CONTACT LENS CLEANING SOLUTION BASED ON QUATERNARY AMMONIUM PHOSPHATE ESTERS

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Field of the Invention

The present invention generally relates to a composition for and a method of cleaning and disinfecting contact lenses and more particularly relates to an improved composition for a contact lens cleaning and disinfecting solution containing a non-ionic surfactant and a triquaternary phosphate ester and a method of using the solution.

10

Background of the Invention

In the normal course of wearing and caring for contact lenses, the process of cleaning, disinfecting, and rinsing are necessary to ensure the ocular health 15 of the contact lens wearer. The rapid development of various types of contact lenses during the past twenty years, i.e., hard contact lens, gas permeable contact lens, soft contact lens made of either hydrophobic or hydrophilic materials, has led to a variety of contact lens care solutions being developed for the consumer market. In most instances, a different solution must be used for 20 each of the individual steps of cleaning, disinfecting, storing, and rinsing before the lenses are ready to be inserted into the eye.

It is desirable for those providing lens care solutions to develop a single solution that can be used to clean, disinfect/store, and rinse contact lenses in a single operation. Such a solution would enable a contact lens wearer to remove 25

a pair of contact lenses from a storage container and insert them into the eyes. directly. One such solution was disclosed in U.S. Patent No. 3,882,036 and U.S. Patent No. 3,954,644, both to Krezanoski, et al. It is intended for use in the cleaning, storing and wetting of flexible silicone contact lenses. It contains a polyoxyethylene/polyoxypropylene block copolymer having a molecular weight between 1900 and 15,500, a microbial growth inhibitor of benzalkonium chloride, purified water and a sufficient amount of at least one essentially neutral, water-soluble compatible salt to provide a solution salt content equivalent to about 0.5% to 1.8% (w/v) sodium chloride. The solution may 30 optionally contain bisodium or trisodium ethylenediamine tetraacetate and a polymeric viscosity-building agent. However, Krezanoski, et al. employed benzalkonium chloride as the anti-microbial agent which when combined with the 35

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surfactant of polyoxyethylene/polyoxypropylene block copolymer has been found to be not completely effective in its anti-microbial activities.

U.S. Patent No. 4,504,405 to Howes discloses a substantially isotonic aqueous solution suitable for the cleaning of soft and gas permeable contact lenses comprising a sterile aqueous solution of 0.01% to 2.00% of an ophthalmically acceptable non-ionic surface active agent, 0.0012% to 0.003% of a chlorhexidine salt and sufficient amount of non-ionic tonicity adjusting agent. The solution taught by Howes may preferably include a non-ionic surface active agent of polyoxyethylene/polyoxypropylene block copolymer. However, Howes does not teach the use of the desirable triquaternary phosphate ester anti-microbial agent.

U.S. Patent No. 4,908,147 to Tsao, et al. discloses an aqueous self-preserving soft contact lens solution containing between 0.005% to 2.0% by weight of a water-soluble amphoteric surfactant; between 0% to 5% by weight of a substantially non-ionic surfactant which may suitably be a polyoxyethylene/polyoxypropylene block copolymer; between 0% to 5% by weight of a thickener; between 0% to 1% by weight of a chelating agent; between 0% to 2% by weight of a buffer; between 0% to 2% by weight of a water-soluble salt compatible with ocular tissue, and the remainder water. The purpose of Tsao, et al.'s composition is to preserve and clean soft contact lenses by using an effective surfactant and a preservative of the amphoteric compound. It does not provide a single step from storage - to the eye solution.

A commercial lens care solution is supplied by I.C.N. Corporation under the trade name of Unicare Green®. This commercially available lens care solution contains a polyoxyethylene/polyoxypropylene copolymer non-ionic surfactant "F127" having a molecular weight of 12,600 and containing 70% polyoxyethylene and 30% polyoxypropylene and a triquaternary phosphate ester anti-microbial agent. The solution has poor cleaning properties. The solution also has a poor anti-microbial activity in a six hour log reduction test against *S. marcescens*. Detailed information about the polyoxyethylene/polyoxypropylene copolymer non-ionic surfactant may be found in a technical pamphlet published by BASF Corporation (Parsippany, N.J.) "Pluronic® & Tetronic® Surfactants" (1989).

It is therefore an object of the present invention to overcome the various drawbacks associated with the use of prior art lens cleaning solutions.

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It is another object of the present invention to provide a single solution for the cleaning, disinfecting, and rinsing of contact lenses by using a unique combination of a non-ionic surfactant and an anti-microbial agent.

It is yet another object of the present invention to provide a cleaning, 5 disinfecting, and rinsing solution for contact lenses containing a non-ionic surfactant having low molecular weight for enhanced cleaning capability and an anti-microbial agent.

It is a further object of the present invention to provide a cleaning, disinfecting, and rinsing solution for contact lenses containing a non-ionic 10 surfactant having low molecular weight for enhanced cleaning property and an anti-microbial agent of triquaternary phosphate ester such that a potentiating reaction between the surfactant and the anti-microbial agent occurs to produce greatly improved anti-microbial activity.

It is another further object of the present invention to provide a cleaning, 15 disinfecting, and rinsing solution for contact lenses that has superior cleaning capability, greatly improved anti-microbial activity, and low cytotoxicity.

It is yet another further object of the present invention to provide a method of cleaning, disinfecting, and rinsing contact lenses with a single solution comprising a non-ionic surfactant of polyoxyethylene/polyoxypropylene block 20 copolymer and a triquaternary phosphate ester.

Summary of the Invention

In an attempt to develop a single solution for the cleaning, disinfecting, and rinsing of contact lenses, the inventors have accidentally and unexpectedly discovered that by the unique combination of a low molecular weight non-ionic 25 surfactant and a triquaternary phosphate ester, the resulting solution not only has superior cleaning property but also has greatly improved anti-microbial activity.

In accordance with a preferred embodiment of the present invention, a 30 cleaning, disinfecting, and rinsing solution for contact lenses having superior cleaning and anti-microbial properties can be formulated. This solution preferably comprises between about 0.1% to about 1.0% (w/v) of a non-ionic surfactant of polyoxyethylene/polyoxypropylene block copolymer having a molecular weight less than 13,000 daltons, a polyoxypropylene to polyoxyethylene weight ratio between 20/80 and 80/20 and a polyoxypropylene molecular weight range of 35 2000 to 3000 daltons; between about 0.001% to about 0.05% (w/v) of a

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triquaternary phosphate ester; between about 0.1% to about 0.9% (w/v) of a neutral, water-soluble salt; between about 0.05% to about 0.10% (w/v) of a chelating agent such as disodium edentate; between about 0.1% to about 0.4% (w/v) of a buffering agent of sodium borate; between about 0.4% to about 1.0% (w/v) of another buffering agent of boric acid, and between about 0.2% to about 0.8% (w/v) of a polymeric thickener of hydroxyethylcellulose (HEC).

5 (w/v) of another buffering agent of boric acid, and between about 0.2% to about 0.8% (w/v) of a polymeric thickener of hydroxyethylcellulose (HEC).

10 The resulting cleaning and disinfecting solution has superior cleaning capability and greatly improved anti-microbial activity due to what is believed to be a potentiating reaction between the non-ionic surfactant and the triquaternary phosphate ester anti-microbial agent.

15 The present invention is also directed to a method of cleaning, disinfecting, and rinsing contact lenses comprising the steps of mixing a non-ionic surfactant of polyoxyethylene/polyoxypropylene block copolymer having a molecular weight range between about 2500 to 13,000 daltons, a polyoxypropylene to polyoxyethylene weight ratio between 20/80 and 80/20 and a polyoxypropylene molecular weight range of 2000 to 3000 daltons; and an anti-microbial agent preferably of triquaternary phosphate ester. A contact lens is then contacted with the solution for a sufficient length of time so that the lens is cleaned, disinfected, and rinsed.

20 **Detailed Description of the Invention**

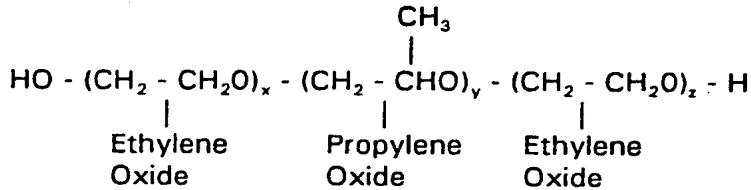
25 The present invention is directed to a new and improved cleaning, disinfecting, and rinsing solution for contact lenses which exhibits superior cleaning capability and greatly improved anti-microbial activity. More specifically, the unexpected effect of potentiation between the non-ionic surfactant and the anti-microbial agent makes this solution extremely effective in killing *S. marcescens* (ATCC 14041). The present invention is further directed to an effective method of cleaning, disinfecting, and rinsing contact lenses in a single step.

30 The present invention can be readily employed with all contact lenses such as conventional hard, soft, gas permeable and silicone lenses. However, it is preferably employed with soft contact lenses such as those commonly referred to as hydrogel lenses prepared by monomers such as hydroxyethylmethacrylate, hydroxyethylmethyl methacrylate, vinylpyrrolidone, glyceromethacrylate, methacrylate or acid esters and the like.

- 5 -

In our preferred embodiment, the present invention involves a new and improved solution for cleaning, disinfecting, and rinsing contact lenses comprising an unique combination of a non-ionic surfactant and a triquaternary phosphate ester anti-microbial agent.

5 In order to produce a solution that is ophthalmically safe to the contact lens user, a family of surfactants of non-ionic nature has been employed in the present invention. A suitable family of surfactants for the present invention can be obtained commercially from the BASF Corporation under the trade name of Pluronic® surfactants. This family of block copolymers can be generally
10 described as polyoxyethylene/polyoxypropylene condensation polymers terminated in primary hydroxyl groups. They are synthesized by first creating a hydrophobe of desired molecular weight by the controlled addition of propylene oxide to the two hydroxyl groups of propylene glycol. In the second step of the synthesis, ethylene oxide is added to sandwich this hydrophobe between
15 hydrophilic groups where the length of the hydrophilic molecules are controlled to constitute between 10% to 80% by weight of the final weight of the molecule. This family of surfactants may be represented by the empirical formula
20



25 where the surfactants may exist in liquid, paste or solid form depending on the molecular weight and the composition ratio of hydrophilic (polyoxyethylene) to hydrophobe (polyoxypropylene).

30 In accordance with a preferred embodiment of the invention, surfactants having lower molecular weights were found to be more efficient cleaning agents. A molecular weight range between about 2500 to 13,000 daltons is a suitable range for our invention. Specific examples of Pluronic® surfactants are satisfactory: L64, F68, F87, F88, F98, P65, P75, P84, P85, P104, and P105.
35 In general, the surfactants of the present invention have a molecular weight of 2500-13,000 daltons, a hydrophobe/hydrophilic ratio range of 80/20 to 20/80 and a hydrophobe molecular weight ranging from about 2000-3000 daltons. The physical properties of these Pluronic® surfactants are listed in

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Table I.

Pluronic®	Avg. Mol. wt, daltons	Melt/Pour Point, °C	Viscosity, CPS (Brookfield) @ 60°C	Surface Tension dynes/cm @25°C, 0.1%	Foam Height - mm (01.% aqueous @ 50° C)
5	P65	3400	27	180	46
	P75	4150	27	250	43
	P84	4200	34	280	42
	P85	4600	34	310	42
10	L64	2900	16	850	43
	F68	8400	52	1000	50
	F87	7700	50	700	44
	F88	11,400	54	2300	48
15	F98	13,000	58	2700	43
					40

TABLE I

15

A suitable concentration range for the Pluronic® surfactants in order to produce satisfactory cleaning is generally 0.01 to 10% (w/v) and preferably between about 0.1% to about 1.0% (w/v). To function satisfactorily in our new and improved solution, the molecular weight of the surfactant should fall in between about 2500 to about 13,000 daltons (preferably 3400 to 6500) and the composition ratio between polyoxypropylene to polyoxyethylene is between about 20/80 to about 80/20 and preferably 40/60 to 60/40. By composition ratio, we mean the ratio of the weight of polyoxypropylene to the weight of polyoxyethylene contained in the surfactant. Preferably, the molecular weight of the polyoxypropylene ranges from 2000 to 3000 daltons, preferably 2330 to 2750 daltons.

20

25

30

Of the different surfactants employed in the present invention, Pluronic® P65, P75 and P85 all have a composition ratio of 50/50 for polyoxypropylene/polyoxyethylene. There is an equal amount of hydrophile and hydrophobe in these surfactants. Another Pluronic® surfactant P84 employed in the present invention has a polyoxypropylene to polyoxyethylene ratio of 80/20. It is reasonable to believe that other surfactants having a polyoxypropylene to polyoxyethylene appropriate ratio should work equally well in our invention.

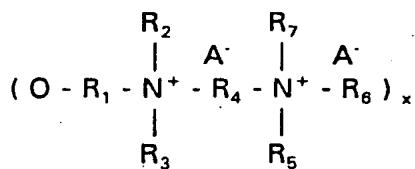
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It is believed that when the hydrophobe content is too high, i.e., above 80%, or the molecular weight of the surfactant is above 13,000 daltons, the surfactant becomes too cytotoxic to be used in a lens care solution. On the other hand, when the hydrophobe concentration is too low, i.e., below 20%, or 5 the molecular weight of the surfactant is below 2500 daltons, the cleaning efficiency of the solution is believed to be reduced. It is also important that the molecular weight of the polyoxypropylene be between about 2000 and about 10 3000 daltons. This was shown to be the case in an ineffective prior art product of Unicare Green® in which Pluronic® F127 was used which contains polyoxypropylene having a molecular weight of 4000 daltons. The preferred and optimal composition of hydrophobe/hydrophile in the surfactant of the present invention is between about 80/20 to about 20/80, and 50/50, respectively.

Another significant aspect of the present invention is the preferred use of a specific microbicidal agent of a triquaternary phosphate ester of cocoamidopropyl PG dimonium chloride phosphate. This triquaternary phosphate ester is commercially available as Phospholipid® PTC (previously known as Monaquat® PTC) supplied by Mona Industries. This triquaternary phosphate ester has good, broad spectrum in its anti-bacteria properties. Unlike other quaternary ammonium compounds, it also has considerable anti-fungal activity 20 in the concentration range of about 100 to about 300 ppm calculated as active solids. The anti-fungal activity of the triquaternary phosphate ester makes it potentially useful when combined with other preservatives such as WSCP (water soluble cationic polymer), etc., to provide full spectrum microbicidal activity with reduced cytotoxicity. In this regard it is particularly noteworthy that WSCP is 25 not very active against *S. marcescens*, but as Pluronic® P85 is added, a sufficient improvement in the microbicidal activity is achieved.

While the lower end of the concentration of Phospholipid® PTC is about 100 ppm, it is possible to lower the concentration to about 10 ppm by adding other preservatives such as benzyl alcohol or potentiating agents.

30 The presently useful water soluble cationic polymers preferably have the following repeating unit



35

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wherein R₁, R₄ and R₆ are each independently selected from alkylene radicals containing 1 to about 6 carbon atoms, R₂, R₃, R₅ and R₇ are each independently selected from alkyl radicals containing 1 to about 6 carbon atoms, each A⁻ is independently selected from ophthalmically acceptable anions, and x is the number of repeating units in the polymer and is an integer in the range of about 5 to about 30.

A specific example of WSCP is poly [oxyethylene (dimethyliminio) ethylene - (dimethyliminio) ethylene dichloride] ("WSCP(1)") as shown below.

10

$$\text{Cl}-\text{CH}_2-\text{CH}_2-(\text{O}-\text{CH}_2-\overset{\text{CH}_3\text{Cl}}{\underset{\text{CH}_3}{\text{N}^+}}-\text{CH}_2-\overset{\text{CH}_3\text{Cl}^-}{\underset{\text{CH}_3}{\text{N}^+}}-\text{CH}_2-\text{CH}_2)_{14}-\text{N} \begin{cases} \text{CH}_3 \\ \text{CH}_3 \end{cases}$$

15 WSCP disinfecting agents are commercially available from Buckman Laboratories, Inc. and are described in U.S. Patent No. 4,250,269 which is incorporated herein by reference.

Monaquat® PTC may be empirically represented by the formula

20

$$[R - CONH - CH_2 - CH_2 - CH_2 - N^{\oplus} - CH_2 - CH - CH_2O]_3 - P + 3 Cl^-$$

$$\begin{array}{c} CH_3 \\ | \\ CH_3 \end{array}$$

$$\begin{array}{c} OH \\ | \\ OH \end{array}$$

$$\begin{array}{c} O \\ || \end{array}$$

B = C = C Alkyl

30 Monaquat® PTC offers excellent substantivity, lubricity and feel to human hair and skin. It is adequately described in U.S. Patent No. 4,209,449 which is incorporated herein by reference.

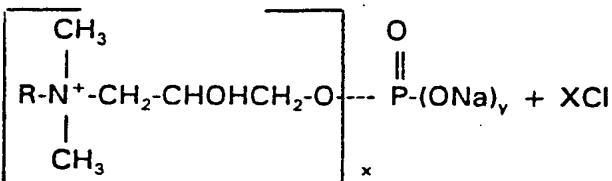
Phospholipid® PTC is a synthetic, vegetable derived multicationic phospholipid complex. It can be obtained from Mona Industries, Inc. of Paterson.

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New Jersey. Its CTFA description is cocamidopropyl PG-Dimonium chloride phosphate with the formula:

5



10

$\text{R} = \text{cocamidopropyl}; x + y = 3$

15

Another disinfecting agent is the poly quaternary amine Croquat L. Croquat L is a quaternary ammonium substituted polypeptide which is based on a collagen hydrolysate of relatively low molecular weight, includes lauryl trimethyl ammonium chloride groups and has a molecular weight in the range of 500 to

about 5000. Croquat L is commercially available from Croda, Inc.

20

To make the present solution more physiologically compatible with the human eyes, it is desirable to make the solution isotonic with human body fluids, that is, the solution should be formulated to contain the same salt concentration as that present in human body fluids. A neutral, water-soluble salt of sodium chloride is employed for this purpose. Other neutral, water-soluble salts such as potassium chloride may also be suitably used.

25

The solution in the present invention also contains a salt of ethylenediamine tetraacetate such as disodium EDTA. This salt is useful as a chelating agent and also as an anti-microbial aid. Other salts suitable for the present invention are sodium hexametaphosphate, sodium citrate, and other chelating agents.

30

Other additives such as buffering agents are used in the present invention to adjust pH value of the solution at a desirable level of 8 or below. A preferred level of pH in the present invention is between about 6.9 and about 7.9. The buffering agents used are boric acid and sodium borate. Other similar acids including, but not limited to, tricine may be suitably used to bring the pH value

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of the solution to a desired level. It is also believed that the borate buffer facilitates antifungal activity.

A viscosity-enhancing agent is also employed in the present invention to bring the viscosity of the solution to a desirable value to provide cushioning of
5 the contact lens in the eye and thus improving comfort to the wearer. A desirable viscosity-enhancing agent for the present invention is HEC (hydroxyethyl cellulose). Other polymeric cellulosic material such as hydroxyethyl methyl cellulose or polymeric non-ionic thickeners such as HPMC (hydroxypropyl methylcellulose), HPC(hydroxypropyl cellulose)and PVA(polyvinyl acetate, with buffers other than the boric acid system) may also be suitably
10 used.

The following examples 1 through 5 are different embodiments of the present invention.

EXAMPLE 1. A cleaning, disinfecting, and rinsing solution for contact
15 lenses is prepared with the following composition.

Boric acid	0.80% (w/v)
Sodium Borate	0.20% (w/v)
Sodium Chloride	0.30% (w/v)
EDTA	0.05% (w/v)
20 Pluronic® P85	0.50% (w/v)
Phospholipid® PTC	0.03% (w/v)
HEC	0.50% (w/v)

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EXAMPLE 2. A new and improved cleaning, disinfecting, and rinsing solution is prepared by the following composition.

Boric Acid	0.80% (w/v)
Sodium Borate	0.20% (w/v)
Sodium Chloride	0.30% (w/v)
EDTA	0.10% (w/v)
Pluronic® P85	0.50% (w/v)
Phospholipid® PTC	0.03% (w/v)
HEC	0.50% (w/v)

10

This solution is similar to that in Example 1 except the content of EDTA is doubled. As will be shown later in Table II, it has improved microbicidal activity against *S. marcescens* at 6 hours and against *A. fumigatus* at 4 hours.

15 EXAMPLE 3. A new and improved cleaning, disinfecting, and rinsing solution for contact lenses is formulated by the following composition:

Boric Acid	0.80% (w/v)
Sodium Borate	0.20% (w/v)
Sodium Chloride	0.30% (w/v)
EDTA	0.05% (w/v)
Pluronic® P85	0.50% (w/v)
Phospholipid® PTC	0.035% (w/v)
HEC	0.50% (w/v)

20

25 This solution is similar to that in Example 1 except the content of Phospholipid® PTC was increased from 0.03% to 0.035%.

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EXAMPLE 4. A cleaning and disinfecting solution for contact lenses is formulated by the composition:

Boric Acid	0.80% (w/v)
Sodium Borate	0.20% (w/v)
5 Sodium Chloride	0.30% (w/v)
EDTA	0.05% (w/v)
Pluronic® P85	0.50% (w/v)
Phospholipid® PTC	0.04% (w/v)
HEC	0.50% (w/v)

10

This example is similar to that in Example 4 except that the content of Phospholipid® PTC is increased from 0.035% to 0.04%.

15 EXAMPLE 5. A cleaning, disinfecting, and rinsing solution for contact lenses is formulated by the composition:

Boric Acid	1.00% (w/v)
Sodium Borate	0.20% (w/v)
Sodium Chloride	0.30% (w/v)
EDTA	0.05% (w/v)
20 Pluronic® P85	0.50% (w/v)
Phospholipid® PTC	0.03% (w/v)
HEC	0.50% (w/v)

20

25

This solution is essentially the same as that in Example 1 except the boric acid content is increased from 0.8% (w/v) to 1.0% (w/v).

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EXAMPLE 6. This example is a commercially available lens care solution supplied by ICN Corporation under the trade name of Unicare Green®. It has the following composition:

	Boric Acid	1.00% (w/v)
5	Sodium Borate	0.20% (w/v)
	Sodium Chloride	0.30% (w/v)
	EDTA	0.10% (w/v)
	Pluronic® F127	0.40% (w/v)
	Phospholipid® PTC	0.03% (w/v)
10	HPMC	0.50% (w/v)

This commercial product uses Pluronic® F127 instead of P85 used in the present invention and HPMC (hydroxypropyl methyl cellulose) instead of HEC used in the present invention.

To test the efficacy in the microbicidal activities of the above examples, a standard log reduction test on three bacteria of *S. marcescens*, *A. fumigatus* and *A. niger* was conducted. This standard log reduction test is expressed in the units of log reduction in a number of contaminating organisms. A ten-fold reduction in the number of contaminating organisms is a one-log reduction. For example, reducing a contamination level of 1,000,000 organisms to 100,000 organisms is a one-log reduction. Reducing a contamination level of 10,000 organisms to 1,000 organisms is also a one-log reduction. It is desired based on worldwide preservation and disinfection criteria that after six hours exposure to the disinfection solution, the bacteria should be reduced by at least three logs and the fungi should be reduced by at least one log. It should be noted that this 20 test is a log reduction from a six-log challenge. Therefore, a requirement for a 25

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three-log reduction means that the solution must be able to reduce a challenge of 10^6 organisms to 10^3 organisms in the required time period.

Microbiological studies were conducted on six solutions, i.e., five solutions formulated by the present invention and one prior art solution. The solutions 5 were tested for anti-microbial kill at four and six hours against the following bacteria and fungi among others, *S. marcescens*, *A. niger*, and *A. fumigatus*. *S. marcescens* is a gram negative, pigmented bacteria, which is one of the most common and resistant contaminant in contact lens care. For a more complete description of the standard method for log kill determination, see Pflug IJ, 10 Holcomb R.G. "Principles of Thermal Destruction of Microorganisms"; Block SS, ed. *Disinfection, sterilization, and preservation*, 3rd ed., Philadelphia, Lea & Febiger, 1983: 751-810; Houlby R.D. "An Alternative Approach for Preservative Testing of Ophthalmic Multiple-Dose Products", *J. Parenter Drug Assoc.*, 1980; 15 34 (4) 272-6.

15 The results of these microbiological studies are shown in Table II.

Organism and Inoculum size	Contact Time	Example 1	Example 2	Example 3	Example 4	Example 5	Example 6
<i>S. marcescens</i>	4 hours	4.60	4.60	>4.90	>4.90	>4.90	0.60
8×10^6	6 hours	4.90	>4.90	>4.90	>4.90	>4.90	1.90
<i>A. Fumigatus</i>	4 hours	1.30	1.48	0.88	1.18	1.18	1.48
6×10^6	6 hours	1.48	1.48	1.48	1.30	1.48	1.48
<i>A. Niger</i> 3×10^6	7 days	1.70	1.48	1.48	1.70	1.70	1.63

25

TABLE II

These results show no significant difference between the six solutions when tested against *A. fumigatus* and *A. niger*. The data show a 1.3 to 1.48 log reduction in 6 hours. However, there is a significant difference between 30 solutions when tested against *S. marcescens*. All solutions in the present invention (Examples 1 through 5) have greater than 4.5 log reduction at 4 hours while the Unicare Green® solution (Example 6) only showed a 0.6 log reduction.

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More significantly, the results showed that all the solutions in the present invention have far superior microbicidal activity against *S. marcescens* than the Unicare Green® solution. This is apparently attributed to the use of the surfactants of the present invention instead of the Pluronic® F127 utilized in the
5 Unicare Green® solution. The results after 6 hours achieved by the present invention is a 4.9 log reduction when compared to a 1.9 log reduction achieved by the Unicare Green® product. The 3 log difference represents that the disinfecting function of the present invention is 1,000 times more effective than the Unicare Green® solution in the killing of *S. marcescens* bacteria.

10 We believe that the use of the non-ionic surfactants of the present invention greatly potentiated the microbicidal activity of the anti-microbial agent used. See Table III below which shows use of the surfactants of the present invention (Entry Nos. 1-4, 6, 7 and 9) having superior microbicidal activity against *S. marcescens* than those outside the present invention (Entry Nos. 5
15 and 8).

This effect of potentiation or synergism between the two unique components contributes to not only a greatly improved microbicidal activity of the solution, but also a superior cleaning capability. This is shown by data obtained in a Draves test where a significant improvement from 49 for Unicare
20 Green® (Example 6) to 6.5 for the present invention (Example 1) was observed.

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	INGREDIENTS	1	2	3	4	5	5*	6	7	8	8*	9
	BORIC ACID	0.8										
5	SODIUM BORATE	0.2										
	SODIUM CHLORIDE	0.3										
	EDTA	0.05										
10	PHOSPHOLIPID PTC	0.03										
	HEC	0.4										
15	PLURONIC P85	0.5										
	PLURONIC F 127		0.5									
	PLURONIC L62 LF			0.5								
	PLURONIC L 92				0.5							
20	PLURONIC P 104					0.5	0.5					
	PLURONIC F 77							0.5				
25	PLURONIC F87								0.5			
	PLURONIC P105									0.5	0.5	
	PLURONIC F 68											0.5
	ANTIMICROBIAL ACTIVITY											
	S.m. LOG REDUCTION											
	4 HRS.	5.3	1.6	TK	5.3	3.3	2.3	4.3	4.6	1.7	1.3	TK
	6 HRS.	TK	2.6	TK	TK	4.3	2.7	TK	TK	**	2.3	TK

Repeat
** Unclear

TABLE III

A desirable range of the present novel invention is shown as follows:

30	Boric Acid	0.4 - 1.00% (w/v)
	Sodium Borate	0.1 - 0.40% (w/v)
	Disodium Edentate	0.01 - 0.10% (w/v)
	Sodium Chloride	0.1 - 0.90% (w/v)
	Pluronic® P85	0.1 - 1.00% (w/v)
35	Phospholipid® PTC	0.01 - 0.05% (w/v)
	HEC	0.20 - 0.80% (w/v)

While several embodiments of the present invention have been shown and described, other embodiments will be apparent to those skilled in the art. Accordingly, the invention is defined only by the following claims.

What is claimed is:

1. A contact lens cleaning, disinfecting, and rinsing solution comprising a surfactant of a block copolymer of polyoxypropylene and polyoxyethylene having a composition ratio of between about 80/20 to about 20/80 and an anti-microbial agent.
- 5 2. The solution according to claim 1 wherein said block copolymer of polyoxypropylene and polyoxyethylene has a composition ratio of 50/50.
3. The solution according to claim 1 wherein said block copolymer of polyoxypropylene and polyoxyethylene further has a molecular weight range 10 between about 2500 to about 13,000 daltons.
4. The solution according to claim 1 wherein said anti-microbial agent is a triquaternary phosphate ester.
5. The solution according to claim 1 wherein there is present in the solution from about 0.01% (w/v) to about 10% (w/v) of the surfactant.
- 15 6. The solution according to claim 1 wherein there is present in the solution from about 0.001% (w/v) to about 0.05% (w/v) of the anti-microbial agent.
7. The solution according to claim 1 wherein there is present in the solution from about 0.01% (w/v) to about 0.10% (w/v) of an alkalinity enhancer.
8. The solution according to claim 1 wherein there is present in the solution 20 from about 0.1% (w/v) to about 0.9% (w/v) of a neutral, water-soluble salt.
9. The solution according to claim 1 further comprising from about 0.2% (w/v) to about 0.8% (w/v) of a viscosity enhancing agent.
10. The solution according to claim 1 wherein there is present in the solution from about 0.1% (w/v) to about 1.0% (w/v) of a block copolymer of 25 polyoxypropylene and polyoxyethylene having a composition ratio of about 50/50 and a molecular weight of about 4600 daltons, from about 0.001% (w/v) to about 0.05% (w/v) of cocoamidopropyl PG dimonium chloride phosphate, from about 0.4% (w/v) to about 1.0% (w/v) of boric acid, from about 0.1% (w/v) to about 0.4% (w/v) of sodium borate, from about 0.01% (w/v) to about 30 0.10% (w/v) of disodium edetate, from about 0.1% (w/v) to about 0.9% (w/v) of sodium chloride, and from about 0.2% (w/v) to about 0.8% (w/v) of hydroxyethyl cellulose.

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11. A method of cleaning and disinfecting a contact lens comprising the steps of:

5 forming a solution comprising a non-ionic surfactant of a block copolymer of polyoxypropylene and polyoxyethylene having a composition ratio of between about 80/20 to about 20/80 and an anti-microbial agent; and

contacting a contact lens with the solution.

12. The method according to claim 11 wherein said block copolymer of polyoxypropylene and polyoxyethylene has a composition ratio of 50/50.

- 10 13. The method according to claim 11 wherein said block copolymer of polyoxypropylene and polyoxyethylene further has a molecular weight range between about 3400 to about 6500 daltons.

14. The method according to claim 11 wherein said anti-microbial agent is a triquaternary phosphate ester.

- 15 15. The method according to claim 11 wherein there is present in the solution from about 0.01% (w/v) to about 10% (w/v) of the surfactant.

16. The method according to claim 11 wherein there is present in the solution from about 0.01% (w/v) to about 0.05% (w/v) of the anti-microbial agent.

- 20 17. The method according to claim 11 wherein there is present in the solution from about 0.01% (w/v) to about 0.1% (w/v) of a chelating agent.

18. The method according to claim 11 wherein there is present in the solution from about 0.1% (w/v) to about 0.9% (w/v) of a neutral, water-soluble salt.

19. The method according to claim 11 wherein the solution further comprising from about 0.2% (w/v) to about 0.8% (w/v) of a viscosity enhancing agent.

- 25 20. The method according to claim 11 wherein there is present in the solution from about 0.1% (w/v) to about 1.0% (w/v) of a block copolymer of polyoxypropylene and polyoxyethylene having a composition ratio of about 50/50 and a molecular weight of about 4600 daltons, from about 0.01% (w/v) to about 0.05% (w/v) of cocoamidopropyl PG dimonium chloride phosphate,

- 30 from about 0.4% (w/v) to about 1.0% (w/v) of boric acid, from about 0.1% (w/v) to about 0.4% (w/v) of sodium borate, from about 0.01% (w/v) to about 0.10% (w/v) of disodium edentate, from about 0.1% (w/v) to about 0.9% (w/v) of sodium chloride, and from about 0.2% (w/v) to about 0.8% (w/v) of hydroxyethyl cellulose.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 94/07347

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C11D3/00 A61L2/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C11D A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US,A,4 510 065 (G.J.SHERMAN) 9 April 1985 see column 4, line 11 - line 15 see column 5, line 12 - line 16 see column 5, line 32 - line 43 see column 8, line 49 - line 51 --- X US,A,3 882 036 (J.Z.KREZANOSKI ET AL.) 6 May 1975 cited in the application see column 7, line 64 - line 68 see column 8, line 1 - line 39 see column 8, line 58 - line 64 see examples 1,5,6 see claims 1-3 --- -/-	1-3,5-9, 11-13, 15-19 1-3,5-9, 11-13, 15-19

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *'A' document defining the general state of the art which is not considered to be of particular relevance
- *'E' earlier document but published on or after the international filing date
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- *'O' document referring to an oral disclosure, use, exhibition or other means
- *'P' document published prior to the international filing date but later than the priority date claimed

- *'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- *&* document member of the same patent family

1

Date of the actual completion of the international search 26 October 1994	Date of mailing of the international search report 13.12.94
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Pelli Wablat, B

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 94/07347

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US,A,3 954 644 (J.Z.KREZANOSKI ET AL.) 4 May 1976 cited in the application see column 8, line 16 - line 28 see column 8, line 58 - line 65 see column 10, line 30 - line 51 see example 1 ---	1-3,5-9, 11-13, 15-19
X	US,A,4 356 100 (G.J.SHERMAN) 26 October 1982 see column 3, line 26 - line 34 see column 4, line 30 - line 33 ---	1-3,5-9
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P,A	WO,A,93 13750 (ALLERGAN INC.) 22 July 1993 see page 6, paragraph 2-3 see page 7, paragraph 3-4 ---	1-9
A	WO,A,89 01023 (INTERFACE RESEARCH CORPORATION) 9 February 1989 see the whole document -----	1-9

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Information on patent family members

International application No.

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International application No.

US 94/07347

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